REGULATION OF THE BLOOD CHOLESTEROL

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Information has been obtained in recent years showing the importance of heparin and heparin-like substances in the regulation of the cholesterol content of the blood [17]. Some workers [15, 17] believe that in atherosclerosis the heparin activity is reduced. Ray, Basu and Stewart [15] point out a correlation between the heparin activity and the lipid content of the blood plasma.

The discovery of the clearing factor and the elucidation of its relationship to heparin emphasize the importance of changes in the physicochemical properties of the blood lipids in the development of hypercholesteremia – the leading sign of a disturbance of the cholesterol metabolism. The action of the clearing factor and of the heparin-like substances is to promote hydrolysis of lipoproteins and to clear the blood plasma of its fatty acids.

The aim of the present investigation was to examine the influence of heparin on the retention of cholesterol in the brain, as an organ with a higher cholesterol content than the liver, to which is attributed a leading part in the removal of cholesterol from the blood.

The basis for this investigation was provided by the work of S. S. Khalatov [9], who demonstrated the role of lesions of the brains (encephalopathies) in the production of endogenous hypercholesteremia. These findings were confirmed by many experimental investigations [1 – 14].

EXPERIMENTAL METHOD

We carried out experiments on 16 dogs – 11 experimental and 5 control animals, using the method of comparative estimation of the concentration of cholesterol and its fractions in the blood entering and leaving the organ.

Two organs were investigated: the liver – blood was taken from the hepatic artery (entering) and the hepatic vein (leaving), and the brain – blood was taken from the carotid artery (entering) and the jugular vein (leaving).

From dogs under morphine-ether-chloroform anesthesia, blood was taken simultaneously from all the vessels used in the investigation for estimation of the cholesterol, after which the experimental animals were injected intravenously with heparin solution (Heparin Richter) in a dose of 0.01 g per kg body weight, and 15 minutes later blood was again taken from the same vessels. Instead of heparin, physiological saline was injected into the control dogs.

Quantitative estimation of cholesterol and its fractions (total, cholesterol as ester, and free cholesterol) was carried out gravimetrically by the digitonin method, using an electrophotocolorimeter for the colorimetry.

EXPERIMENTAL RESULTS

After the intravenous injection of heparin the concentration of cholesterol in the blood fell in all the vessels examined and in all the experiments.

TABLE 1

Concentration of Cholesterol and Its Fractions in the Serum of Dogs Before and After Injection of Heparin (mean values of 11 experiments)

Name of vessel	Cholesterol content in mg%								
	total			as ester			free		
	before	after	difference	before	after	difference	before	after	difference
Hepatic artery	116	110	—6	82	80	—2	36	32	—4
Hepatic vein	133	114	—19	87	85	—2	43	29	—14
Carotid artery	118	112	—6	83	81	—2	36	31	—5
Jugular vein	122	108	—14	80	77	—3	41	31	—10

TABLE 2

Concentration of Cholesterol and Its Fractions in the Serum of Control Dogs (mean value of 5 experiments)

Name of vessel	Cholesterol content in mg%								
	total			as ester			free		
	before	after	difference	before	after	difference	before	after	difference
Hepatic artery	120	121	+1	81	82	+1	39	39	0
Hepatic vein	134	135	+1	81	82	+1	53	53	0
Carotid artery	121	121	0	82	81	—1	39	39	0
Jugular vein	128	128	0	83	83	0	45	45	0

TABLE 3

Proportion of Ester and Free Cholesterol as a Percentage of the Total Serum Cholesterol of Dogs Before and After Injection of Heparin

Name of vessel	as ester			free		
	before	after	difference	before	after	difference
Hepatic artery	69	71	+2	31	29	—2
Hepatic vein	68	75	+7	32	25	—7
Carotid artery	69	73	+4	31	29	—2
Jugular vein	67	72	+5	33	28	—5

In the control animals no changes were found in the blood cholesterol after injection of physiological saline (Table 2).

The fall in the blood cholesterol of the experimental animals occurred, as may be seen from Table 1, mainly on account of a fall in the free cholesterol. Whereas normally the free blood cholesterol accounted for 32% of the total in all the vessels examined, after injection of heparin its concentration became 25% in the hepatic vein and 28% in the jugular vein (Table 3).

No changes were observed in the percentage of free cholesterol in relation to the total in the control dogs.

By comparing the degree of reduction of the concentration of cholesterol and its fractions in dogs after injection of heparin, in the blood entering the organ and in that leaving it (Table 1), it may clearly be stated that the fall of both total cholesterol and of its fractions, and in particular of the free cholesterol, was greater in the blood leaving the organ. Whereas the total cholesterol concentration in the blood from the hepatic artery fell by 6 mg% from its initial level of 116 mg%, i.e. by 5%, the total cholesterol in the blood from the hepatic vein fell by 19 mg% from its initial 133 mg%, i.e. by 15%. An even greater degree of difference was shown by the free cholesterol; the free cholesterol in the hepatic artery, for instance, fell by 4 mg% from the initial 36 mg%, i.e. by 11%, whereas the fall in the free cholesterol of the hepatic venous blood was 14 mg% from its initial level of 43 mg%, i.e. 32%.

These findings emphasize the role of the liver in the removal of cholesterol from the blood.

The results obtained in the investigation of the concentration of cholesterol and its fractions in the blood from the carotid artery (entering) and the jugular vein (leaving the brain) suggest that the role of the liver is not an exclusive one in this process and that the brain actively retains cholesterol, and in particular free cholesterol, in its tissue after injection of heparin. For instance, whereas the total cholesterol in the blood from the carotid artery fell by 6 mg% from an initial level of 118 mg%, i.e. by 5%, its concentration in the blood from the jugular vein fell by 14 mg%, i.e. by 11% from the initial 122 mg%. The difference is expressed to an even greater degree in respect of the free cholesterol. In the carotid artery it fell by 5 mg% from the initial 36 mg%, i.e. by 13%, and in the blood from the jugular vein its absolute value fell by 10 mg% from the initial concentration of 43 mg%, i.e. by 24%.

The same relationship was shown in the changes in the proportion of free to total cholesterol; for instance whereas the free cholesterol in the carotid artery fell from 31 to 29% after injection of heparin, in the blood from the jugular vein it fell from 33 to 28%, i.e. by 5%. The results of the investigation lead to the conclusion that the regulation of the blood cholesterol after injection of heparin involves the participation not only of the liver but of the brain also.

The proportionately greater fall in the free cholesterol may be interpreted as showing the greater importance of this fraction of the cholesterol in this particular process.

SUMMARY

Experiments were conducted on 16 dogs, 5 of which were control. A comparative significance of the liver and of the brain in the control of cholesterol in the blood serum in administration of heparin was studied. The method of comparative determination of the total cholesterol and its fractions – ether-combined and free in the inflowing and outflowing blood of the liver and of the brain, was used. A significant decrease of total cholesterol in the blood flowing from the organs was noted. Evidently the blood cholesterol level is controlled not only by the liver, but also by the brain, which is confirmed by the active retention of cholesterol in the brain tissue. Decrease of the blood cholesterol level (as a result of the drop of free cholesterol, i.e. the fraction which equals about 1/3 of the total cholesterol) following the administration of heparin permits to conclude that free cholesterol plays an important role in this process.

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